

pulmonary toxicity from amiodarone is not precisely known, but it is estimated to be 1–5%.¹¹ Although the association of PPFE with amiodarone has not yet been described, given the amount of lung toxicity cases induced by amiodarone, the multiplicity of clinical presentations observed, added to the description of PPFE as a possible pattern associated with lung toxicity induced by drugs, sustain the hypothesis that PPFE can be the expression of lung toxicity induced by amiodarone. Moreover, the symptom regression after the amiodarone suspension and the absence of radiologic changes before the amiodarone prescription support the hypothesis of the association between PPFE and amiodarone intake in this clinical case.

References

1. Amitani R, Niimi A, Kuse F. Idiopathic pulmonary upper lobe fibrosis (IPUF). *Kokyu*. 1992;11:693–9.
2. Frankel SK, Cool CD, Lynch DA, Brown KK. Idiopathic pleuroparenchymal fibroelastosis: description of a novel clinicopathologic entity. *Chest*. 2004;126:2007–13.
3. Travis WD, Costabel U, Hansell DM, King TE, Lynch DA, Nicholson AG, et al. An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med*. 2013;188:733–48.
4. Bonifazi M, Montero MA, Renzoni EA. Idiopathic pleuroparenchymal fibroelastosis. *Curr Pulmonol Rep*. 2017;6:9–15.
5. Khirya R, Macaluso C, Montero MA, Wells AU, Chua F, Kokosi M, et al. Pleuroparenchymal fibroelastosis. *Am J Surg Pathol*. 2017;41:1683–9.
6. Kato M, Sasaki S, Kurokawa K, Nakamura T, Yamada T, Sasano H, et al. Usual interstitial pneumonia pattern in the lower lung lobes as a prognostic factor in idiopathic pleuroparenchymal fibroelastosis. *Respiration*. 2018;6:1–10.
7. Silva JP, Melo N, Guimarães S, Morais A. Pleuroparenchymal fibroelastosis and silicosis: an unexpected association. *Arch Bronconeumol*. 2018;54:529–31.
8. Nunes H, Jeny F, Bouvry D, Picard C, Bernaudin J-F, Ménard C, et al. Pleuroparenchymal fibroelastosis associated with telomerase reverse transcriptase mutations. *Eur Respir J*. 2017;49, 1602022.
9. Camus P, Thu J, Von Der, Hansell DM, Colby TV. Pleuroparenchymal fibroelastosis: one more walk on the wild side of drugs? *Eur Respir J*. 2014;289–96.
10. Reddy TL, Tominaga M, Hansell DM, Von Der Thusen J, Rassl D, Parfrey H, et al. Pleuroparenchymal fibroelastosis: a spectrum of histopathological and imaging phenotypes. *Eur Respir J*. 2012;40:377–85.
11. Papiris SA, Triantafyllidou C, Kolilekas L, Markoulaki D, Manali ED. Amiodarone review of pulmonary effects and toxicity. *Drug Saf*. 2010;33:539–58.

Marcos Oliveira^{a,*}, Natália Melo^b, Patrícia Caetano Mota^{b,c}, Helder Novais e Bastos^{b,c,d}, José Miguel Pereira^e, André Carvalho^e, Susana Guimarães^f, Conceição Souto Moura^f, António Morais^{b,c,d}

^a Pulmonology Department, Unidade Local de Saúde da Guarda, Guarda, Portugal

^b Pulmonology Department, Centro Hospitalar São João, Porto, Portugal

^c Faculdade de Medicina do Porto, University of Porto, Portugal

^d Institute for Research and Innovation in Health (I3S), University of Porto, Portugal

^e Radiology Department, Centro Hospitalar São João, Porto, Portugal

^f Pathology Department, Centro Hospitalar São João, Porto, Portugal

* Corresponding author.

E-mail address: marcosandre.oliveira90@gmail.com (M. Oliveira).

<https://doi.org/10.1016/j.arbres.2019.06.011>

0300-2896/ © 2019 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

Cardiovascular disease in Canary Island patients with chronic obstructive pulmonary disease: “Spicy Sauce for Our Wrinkled Potatoes”[☆]



Patología cardiovascular en el paciente con enfermedad pulmonar obstructiva crónica de las islas Canarias. «El mojo picón de nuestras papas»

To the Editor:

Mojo picón is a typical sauce from the Canary Islands, made from oil, vinegar and red pepper, which gives it its characteristic red color. This spicy sauce, used in the olden days by sailors on the high seas to accompany our famous *papas arrugadas* - wrinkled potatoes - when there was nothing else to eat, is the product of the meeting of different cultures at a time when our islands were a bridge for trade between the Americas, Europe and Africa. Nowadays, when someone from Canary Islands travels abroad, they are immediately associated with this dish, which could almost be seen as their “calling card”. This cultural sauce pot has had its impact not only on gastronomy, but also on the patients of this autonomous community.

Although the Canarian population is considered to be phenotypically Caucasian, their ethnic origins differ from the rest of Spain. The inhabitants of the archipelago are descendants of a mixture of an aboriginal population from northern Africa and European settlers who arrived in the islands in the 15th century.¹ Factors such as the distance from the continent and the geographical features

of the islands themselves led to a tendency towards endogamy over many generations. This, in turn, led to the emergence of rare diseases in specific areas of the region, for example, familial hypertrophic cardiomyopathy² or rare allele variants in alpha-1 antitrypsin deficiency.³ The result of this “genetic selection” is that chronic pathologies such as cardiovascular or respiratory diseases may present in more complex forms in inhabitants of the Canary Islands than in the continental population.^{1,4}

Chronic obstructive pulmonary disease (COPD), for example, is less prevalent in the Canaries than in the rest of Spain,⁵ although several studies seem to suggest that it is more difficult to manage.^{6,7} Patients in the Canaries have a greater comorbidity burden than other Spanish cohorts with a similar degree of obstruction,⁶ complicating their clinical situation. Despite a lower tobacco consumption, these patients show a high prevalence of cardiovascular comorbidity, even at earlier disease stages; reported rates are higher than those described in Spain in general,⁷ in Europe, and in the United States. Of particular interest are a greater presence of hypertension (HT), dyslipidemia, obesity, cardiac arrhythmia, and ischemic heart disease (IHD) (Fig. 1).

Most individuals are prompted to seek medical attention because of dyspnea. This symptom encompasses multiple qualitative and quantitative parameters, and as a result, is manifested in this disease in several different ways. The important role of cardiovascular comorbidities in COPD must also be taken into account. In the Canary Islands, the most symptomatic COPD patients (GOLD 2017 groups B and D) have a 4-fold risk of IHD or heart failure (HF), and a 2-fold risk of cardiac arrhythmia, diabetes mellitus type 2 (DM2), HT and peripheral artery disease.⁸ These results differ from observations reported in other populations: Kahnert et al.⁹ found that in COPD in the United Kingdom, the most symptomatic patients had a risk of IHD of less than 2-fold, and that the risk of

[☆] Please cite this article as: Figueira Gonçalves JM. Patología cardiovascular en el paciente con enfermedad pulmonar obstructiva crónica de las islas Canarias. «El mojo picón de nuestras papas». *Arch Bronconeumol*. 2020;56:57–58.

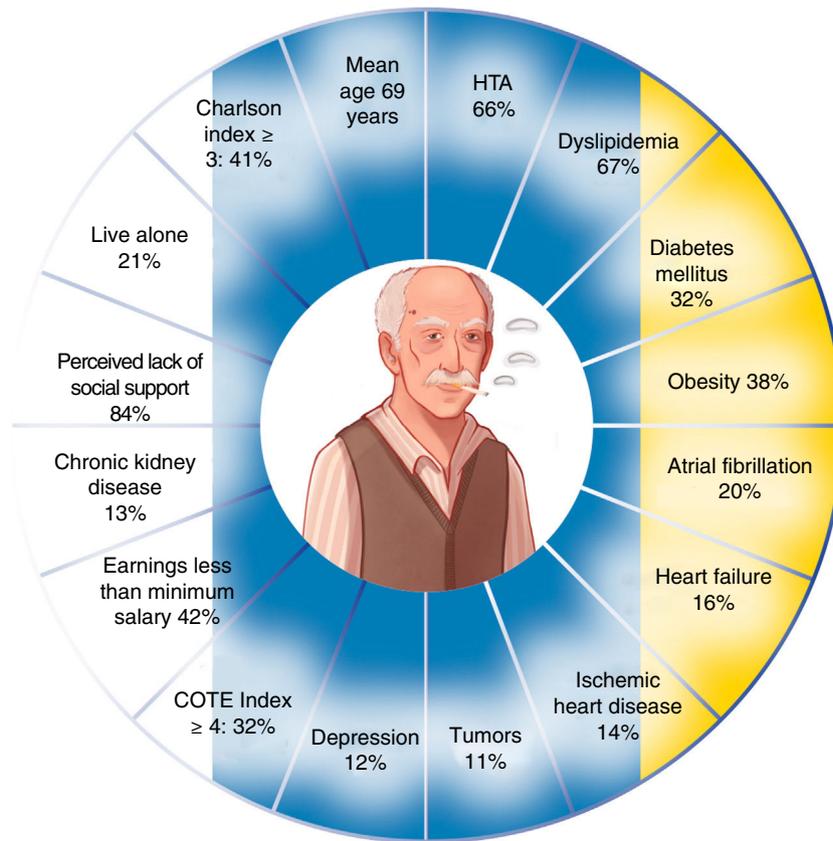


Fig. 1. Characterization of patients with chronic obstructive pulmonary disease in the Canary Islands. Diagram adapted from various studies conducted in the archipelago. COTE: COPD-specific co-morbidity test; HTN: hypertension.

HF, DM2, or HT remained non-significant. These results underline the importance of evaluating cardiovascular disease when monitoring symptoms in Canary Islanders, and highlight the risk of heart disease in subjects with a greater degree of dyspnea and cerebrovascular accident in patients with increased probability of exacerbation.¹⁰

With regard to the risk of hospitalization, results obtained in the Lung Health Study¹¹ showed that up to 42 % of first hospitalizations in patients with mild COPD were due to cardiovascular causes. This must be seen in the light of the results of the SUMMIT study, which determined that the risk of a cardiovascular event after an exacerbation in COPD patients with cardiovascular comorbidity increased by 4-fold in the 30 days after onset, and was as high as 10-fold in patients requiring admission to hospital.¹² A small population-based study conducted in the Canary Islands evaluating the effectiveness of the administration of 13-valent pneumococcal conjugate polysaccharide vaccination in COPD patients with established cardiovascular disease found that the risk of hospitalization for exacerbation in subjects with cardiovascular comorbidity increased up to 9-fold compared to those who did not present this pathology.¹³ Due to the high cardiovascular burden of patients in our islands, these data reinforce the need to establish measures to improve the monitoring of comorbidities and to maximize follow-up in the event of exacerbation.

With regard to the impact of comorbidities on the life expectancy of these patients, a study published by Divo et al.¹⁴ concluded that cardiovascular disease, especially IHD, HF, or cardiac arrhythmia, has a negative impact on the survival of patients with COPD in outpatient follow-up. On the basis of the results of that study, we performed a similar analysis in patients in the Canary Islands, and found that the impact of cardiovascular disease differs

from the findings of those authors, yet chronic kidney disease acquired a special relevance in the community of the Canaries. No significant impact was detected for the presence of IHD,¹⁵ but this may be because this disease is closely and efficiently managed in the archipelago.

The factors discussed here should lead us to reflect on the differences between the COPD population in the Canary Islands and the Iberian peninsula or Europe, and to bear in mind the specific particularities of our patients. Just like our wrinkled potatoes with spicy sauce, this COPD population has its own identity marked by the complexity of its patients, in which the cardiovascular comorbidity/systemic involvement (what we have colloquially dubbed “the Canaries phenotype”) plays a significant role, and where the combination of hypertension, dyslipidemia, DM2, smoking and obesity is part of our day-to-day experience. Given these facts, then, we must be aware of the need for targeted measures aimed at the correct management of these patients with the goal of improving their quality of care.

Acknowledgements

My thanks go to all my colleagues and friends who have supported me in my efforts to characterize the COPD population in the Canary Islands, and I also thank Violeta Ferrer for her illustration.

References

- Guillen-Guio B, Lorenzo-Salazar JM, González-Montelongo R, Díaz-de Usera A, Marcelino-Rodríguez I, Corrales A, et al. Genomic Analyses of Human European Diversity at the Southwestern Edge: Isolation, African Influence and Disease Associations in the Canary Islands. *Mol Biol Evol.* 2018;35:3010–26.
- Cuenca S, Ruiz-Cano MJ, Gimeno-Blanes JR, Jurado A, Salas C, Gomez-Diaz I, et al. Inherited Cardiac Diseases Program of the Spanish Cardiovascular Research Network (Red Investigación Cardiovascular). Genetic basis of familial dilated

- cardiomyopathy patients undergoing heart transplantation. *J Heart Lung Transplant*. 2016;35:625–35.
- [3]. Martínez Bugallo F, Figueira Gonçalves JM, Martín Martínez MD, Díaz Pérez D. Spectrum of Alpha-1 Antitripsin Deficiency Mutations Detected in Tenerife. *Arch Bronconeumol*. 2017;53:595–6.
- [4]. Aragón-Sánchez J, García-Rojas A, Lázaro-Martínez JL, Quintana-Marrero Y, Maynar-Moliner M, Rabellino M, et al. Epidemiology of diabetes-related lower extremity amputations in Gran Canaria, Canary Islands (Spain). *Diabetes Res Clin Pract*. 2009;86:e6–84.
- [5]. Cabrera López C, Juliá Serdá G, Cabrera Lacalzada C, Martín Medina A, Gullón Blanco JA, García Bello MA, et al. Prevalence of chronic obstructive pulmonary disease in the Canary Islands. *Arch Bronconeumol*. 2014;50:272–7.
- [6]. Figueira Gonçalves JM, Golpe R, García Bello MA, García-Talavera I, Castro Añón O. Comparison of the prognostic capability of two comorbidity indices in patients with chronic obstructive pulmonary disease, in real-life clinical practice. *Clin Respir J*. 2019;13:404–7.
- [7]. Figueira Gonçalves JM, Dorta Sánchez R, Rodríguez Pérez MDC, Viña Manrique P, Díaz Pérez D, Guzmán Saenz C, et al. Cardiovascular comorbidity in patients with chronic obstructive pulmonary disease in the Canary Islands (CCECAN study). *Clin Investig Arterioscler*. 2017;29:149–56.
- [8]. Figueira Gonçalves JM, Martín Martínez MD, Pérez Méndez LI, García Bello MA, García-Talavera I, Hernández SG, et al. Health Status in Patients with COPD According to GOLD 2017 Classification: Use of the COMCOLD Score in Routine Clinical Practice. *COPD*. 2018;6:1–8.
- [9]. Kahnert K, Alter P, Young D, Lucke T, Heinrich J, Huber RM, et al. The revised GOLD 2017 COPD categorization in relation to comorbidities. *Respir Med*. 2018;134:79–85.
- [10]. Figueira Gonçalves JM, García Bello MÁ, Martín Martínez MD, Pérez Méndez LI, García-Talavera I, García Hernández S, et al. The COPD comorbidity in the light of the degree of dyspnea and risk of exacerbation. *COPD*. 2019;16:104–7.
- [11]. Miller J, Edwards LD, Agustí A, Bakke P, Calverley PM, Celli B, et al. Comorbidity, systemic inflammation and outcomes in the ECLIPSE cohort. *Respir Med*. 2013;107:1376–84.
- [12]. Kunisaki KM, Dransfield MT, Anderson JA, Brook RD, Calverley PMA, Celli BR, et al. Exacerbations of Chronic Obstructive Pulmonary Disease and Cardiac Events. A Post Hoc Cohort Analysis from the SUMMIT Randomized Clinical Trial. *Am J Respir Crit Care Med*. 2018;198:51–7.
- [13]. Figueira Gonçalves JM, García Bello MA, Bethencourt Martín N, Díaz Pérez D, Pérez-Méndez LI. Impact of 13-valent pneumococcal conjugate polysaccharide vaccination on severe exacerbations in patients with chronic obstructive pulmonary disease and established cardiovascular disease. *Eur J Intern Med*. 2019;63:e14–6.
- [14]. Divo M, Cote C, de Torres JP, Casanova C, Marin JM, Pinto-Plata V, et al. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2012;186:155–61.
- [15]. Figueira Gonçalves JM, García Bello MA, Martín Martínez MD, García-Talavera I, Golpe R. Can the COPD-comorbidity index be applied to all outpatients with chronic obstructive pulmonary disease? A Single-center Analysis. *Arch Bronconeumol*. 2019, pii: S0300-2896(19)30212-1.

Figueira Gonçalves JM*

Servicio de Neumología y Cirugía Torácica, Hospital Universitario Nuestra Señora de la Candelaria (HUNSC), Santa Cruz de Tenerife, Spain

Corresponding author at: Camino Margallo nº 29 Vivienda 4 CP: 38206 San Cristóbal de la Laguna (Santa Cruz de Tenerife), Santa Cruz de Tenerife, Spain.

E-mail address: juanmarcofigueira@gmail.com

<https://doi.org/10.1016/j.arbr.2019.07.004>

1579-2129/ © 2019 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

Cryptococcus neoformans pleuritis in an immunocompetent patient[☆]



Pleuritis por *Cryptococcus neoformans* en paciente inmunocompetente

To the Editor:

The genus *Cryptococcus* includes different species of encapsulated yeast fungi, of which only *C. neoformans* is considered a human pathogen. Its polysaccharide capsule confers virulence by protecting it from phagocytosis and complement activity. Four serotypes within this species have been described – A, B, C, and D – depending on the components of the capsule. Serotypes A and D are identified as *C. neoformans* var. *neoformans*, and antigens B and C as *C. neoformans* var. *gattii*. The 2 varieties differ both in their pathogenesis and their geographical distribution. *C. neoformans* var. *neoformans* is distributed worldwide and is associated with infections in immunocompromised patients, while *C. neoformans* var. *gattii* has been associated with infections in immunocompetent patients, and its distribution is more restricted to tropical and subtropical countries.¹

C. neoformans var. *neoformans* can affect any individual, although it is more common in patients with a predisposing factor (HIV infection, use of immunosuppressive drugs, connective tissue disease, cirrhosis, etc.).²

Despite the fact that the pigeon feces are the most important source of infection, these animals do not suffer from the disease. Humans acquire *Cryptococcus* infection by the respiratory route, and transmission from person to person has not been proven.

[☆] Please cite this article as: Rodríguez-Álvarez A, Fernández-Rial Á, Pérez-López A, Pita J. Pleuritis por *Cryptococcus neoformans* en paciente inmunocompetente. *Arch Bronconeumol*. 2020;56:59–60.

Although the infection tends to enter via the airways, pulmonary involvement is rare, while the most common presentation is neurological. Pulmonary lesions caused by *Cryptococcus* vary, and include nodules, masses, interstitial infiltrates, alveolar consolidation, and lymphadenopathy.^{3,4} Pleural effusion, either isolated or associated with pulmonary disease is a rare manifestation.^{2–6}

We describe a case of pleuritis caused by *C. neoformans* in an immunocompetent patient.

Our patient was a 78-year-old man with a history of chronic kidney disease stage 3a, permanent atrial fibrillation, congestive heart failure with preserved ejection fraction, alcoholic liver disease, and chronic obstructive pulmonary disease/sleep apnea hypopnea syndrome overlap (COPD + SAHS) receiving treatment with CPAP. He attended our clinic due to a 4 or 5-day-history of sudden onset right pleuritic pain, accompanied by increased dyspnea, cough with expectoration of mucus, and low-grade fever in the afternoon. His general status on physical examination was good, with blood pressure 139/68 mmHg, heart rate 83 bpm, axillary temperature 37.5 °C, SatO₂ 95 % baseline. Mobile right axillary lymphadenopathies were detected, with no palpable lymphadenopathies in other territories. Arrhythmias were heard on cardiac auscultation, and pulmonary auscultation revealed reduced breath sounds in the right lung base with bilateral rhonchi; no other significant findings were detected on physical examination.

Clinical laboratory tests were significant for mild anemia and raised inflammatory markers. Chest radiography revealed right pleural effusion.

A diagnostic thoracentesis was performed, and the drained fluid showed biochemical characteristics of exudate: pH 7.45, glucose 121 mg/dl, protein 4.1 g/dl, ADA 24.7 U/l, erythrocytes 25,200 μl, nucleated cells 3100 μl (polymorphonuclear 39 %, lymphocytes 23 %, macrophages 38 %, and reactive mesothelial cells). Pleural fluid, sputum, and blood were collected and sent for culture.

Diuretic treatment with furosemide was intensified and empiric antibiotic coverage started with ceftriaxone. On day 4 of admission,